

U. S. Serial No. 09/776,865
Filed: February 2, 2001
Declaration of Dr. Carl G. Hellerqvist
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Visiting Professor of Biology, Northwest University, P.R. China;

Member of Special Study Section on Angiogenesis, National Cancer Institute/National Heart, Lung and Blood Institute (NCI/NHLBI);

Member of Special Study Section on Molecular Target Drug Discovery for Cancer, NCI.

I earned an M.S. degree in 1967 at Stockholms Universitet (Sweden). I earned a Ph.D. degree in Chemistry in 1967 at Stockholms Universitet (Sweden). My *curriculum vitae* is enclosed (Exhibit A). I published over of one hundred papers in the fields of biochemistry and cancer studies. The list of the publications is enclosed (Exhibit B).

2. I am a sole named inventor on the U.S. Patent Application Serial Number 09/776,865, filed February 2, 2001, (hereinafter referred to as "the present application"), entitled "Methods for Preventing or Attenuating Pathoangiogenic Conditions." I am familiar with the Office Actions mailed by the United States Patent and Trademark Office in the present application on July 16, 2003 and July 26, 2004, and the Final Office Action mailed by the United States Patent and Trademark Office on February 24, 2005. Specifically, I am familiar with the rejection of Claims 1, 4-16, 29-38, 40-48, 55, and 56 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement

3. As one of ordinary skill in the art in the field of the invention, I declare that, in the field of cancer studies, mouse models are considered by those of ordinary skill in the art as reasonably correlating with the human pathoangiogenic conditions, such as cancer. Those of ordinary skill in the art in the field of cancer studies consider mouse models reasonably predictive of the therapeutic utility of compositions and methods for preventing or attenuating pathoangiogenic conditions, such as cancer. Those of ordinary skill in the art in the field of cancer studies, including members of American Association for Cancer Research (AACR), widely use mouse models to assess and reasonably predict utility of anti-cancer vaccines. For example, during AACR 96th Annual Meeting (April 16-20, 2005,

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Anaheim/Orange County, CA) multiple studies using such mouse models were described and discussed (see Exhibits C-D).

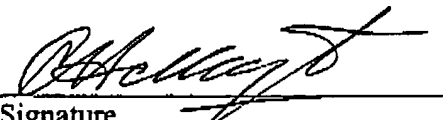
4. The disclosure of the present application enables one of ordinary skill in the art in the field of cancer studies to obtain compositions comprising one or more Group B α -hemolytic *Streptococci* toxin receptors or immunogenic fragments thereof, wherein the GBS toxin receptor comprises HP59 and SP55, and to use the compositions to induce or maintain an immune response in a mammal to at least one of the Group B α -hemolytic *Streptococci* toxin receptors, and to prevent or attenuate development of pathoangiogenic conditions, including cancer, in a mammal. For example, Example 6 of the present application shows that immunization by compositions comprising immunogenic fragments of Group B α -hemolytic *Streptococci* toxin receptors prevents intravenously injected melanoma cells from establishing lethal metastases in the lungs.

5. The publication by Fu *et al.* "Identification of a Novel Membrane Protein, HP59, with Therapeutic Potential as a Target of Tumor Angiogenesis" *Clinical Cancer Research*, v. 7, 4182-4194, (2001) (hereinafter *Fu*) shows that the compositions claimed in the present application can be used to prevent or attenuate pathoangiogenic conditions, such as cancer. In particular, *Fu* supplies evidence that the compositions are effective in preventing angiogenesis and pathology characteristic of cancer. *Fu* shows inhibition of Lewis lung tumor growth and reduction in dissemination and growth of metastases. These are the criteria accepted by those of ordinary skill in the art in the field of cancer studies for characterization of effective prevention or attenuation of cancer. Those of ordinary skill in the art in the field of cancer studies know that Lewis tumors are extremely aggressive. *Fu* demonstrates that immunization with a composition comprising HP59-derived peptides resulted in attenuation or prevention of pathologic angiogenesis and vasculogenesis of Lewis tumors, as demonstrated by immunohistochemistry by the absence of CD34- and HP59-positive vessels.

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6. Compositions comprising HP59-derived peptides are effective in preventing angiogenesis and pathology characteristic of cancer. See, for example, Wamil et al. (2002), "A cancer vaccine based on the pathoangiogenic marker HP59 gives a cellular immune response protecting against repeated intravenous melanoma infusions in mouse models" (enclosed herewith as Exhibit E).

7. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine, or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of any patent issuing on this application.


Signature

Carl G. Hellerqvist, Ph.D.
Name

April 25, 2005
Date



CURRICULUM VITAE

CARL GUSTAF HELLERQVIST

Home address: 2024 Branch Oak Trail
Nashville, Tennessee 37214

Business: Department of Biochemistry
Vanderbilt University School of Medicine
Nashville, Tennessee 37232-0146
Phone: 615-322-4339
Fax: 615-322-6354

Citizenship: U.S.

Education:

1967 Philosophie Kandidat, Stockholms Universitet, (M.S.)
 Scientific Field: Chemistry, Mathematics
1968 Philosophie Licentiat, Stockholms Universitet, (Ph.D.)
 Scientific Field: Chemistry
1971 Philosophie Doktor, Docent, Stockholms Universitet
 Scientific Field: Chemistry, Molecular Biology

Previous Experience:

1967-1978 Instructor, Department of Organic Chemistry, Stockholms Universitet
1969-1971 Assistant Professor, Department of Organic Chemistry, Stockholms Universitet
1971-1972 Visiting Assistant Professor, Department of Biology, The Johns Hopkins
 University, Baltimore, Maryland
1973-1974 Research Scientist, Department of Biology, The Johns Hopkins University,
 Baltimore, Maryland
1974-1981 Assistant Professor, Department of Biochemistry, Vanderbilt University, Nashville,
 Tennessee

Previous Experience: (cont.)

1982-1999	Associate Professor, Department of Biochemistry, Vanderbilt University, Nashville, Tennessee
1980-1984	Director of Graduate Studies, Department of Biochemistry, Vanderbilt University, Nashville, Tennessee
1987-1990	Scientific Advisory Board, Glycomed, Inc., Alameda, CA
1995-1999	Associate Professor, Department of Medicine, Vanderbilt University, Nashville, Tennessee
1999-2001	Director CarboMed Inc
1989-2001	Founder/Consultant, CarboMed, Inc.

Present Positions:

1999-present	Professor, Department of Biochemistry, Vanderbilt University, Nashville, Tennessee
1999-present	Associate Professor, Department of Medicine (Oncology), Vanderbilt University, Nashville, Tennessee
1971-present	Docent, Faculty of Sciences, Stockholms Universitet
1987-present	Investigator, Vanderbilt Center for Lung Research
1994-present	Scientific Advisory Committee, Cambridge Healthtech Institute (New Cancer Strategies)
1994-present	Participating Faculty in Vanderbilt Ingram Cancer Center, Vanderbilt University, Nashville, Tennessee
1997-present	Associate Editor, <i>Angiogenesis</i>
1998-present	Editorial Board, <i>International Journal of Modern Cancer Therapy</i>
1999-present	Visiting Professor of Biology, Northwest University, P.R. China
1999-present	Member, Special Study Section on Angiogenesis, NCI/NHLBI
2000-present	Member special Study Section on Molecular Target Drug Discovery for Cancer
2000-present	Founder, Director and Chief Scientific Officer for AngioPath Inc

Issued Patents:

1. *Therapeutic Agent and Method of Inhibiting Vascularization of Tumors*. C.G. Hellerqvist, U.S. 5,010,062 - April 23, 1991.
2. *Polysaccharide Toxin from Group B b-Hemolytic Streptococcus (GBS) Having Improved Purity*. C.G. Hellerqvist, U.S. 5,811,403 - September 22, 1998.
3. *Facilitation of Wound Healing with CM101/GBS Toxin*. C.G. Hellerqvist, B.D. Wamil, M. Neeman and R. Abramovitch, U.S. 5,858,991 - January 12, 1999.
4. *Methods for Purifying GBS Toxin/CM101*. C. G. Hellerqvist, U.S. 5,939,396 - August 17, 1999.
5. *Facilitation of Repair of Neural Injury with CM101/GBS Toxin*. C.G. Hellerqvist, A.W. Wamil and B.D. Wamil. U.S. 5,981,508 - November 9, 1999.
6. *Treatment of Chronic Inflammatory Diseases with CM101/GBS Toxin*. C.G. Hellerqvist and B.D. Wamil. U.S. 6,028,060 - February 22, 2000.
7. *Polysaccharide Toxin from Group B b-Hemolytic Streptococcus (GBS) Having Improved Purity*. C.G. Hellerqvist. U.S. 6,136,789 - October 24, 2000.
8. *Methods for Purifying GBS Toxin/CM101*. U.S. 6,407,069 - June 18, 2002.
9. *Facilitation of Repair of Neural Injury with CM101/GBS Toxin*. C.G. Hellerqvist, A.W. Wamil and B.D. Wamil. U.S. 6,476,001 - November 5, 2002.
10. *Treatment of Chronic Inflammatory Diseases with CM101/GBS Toxin*. C.G. Hellerqvist and B.D. Wamil.. U.S. 6,476,002 - November 5, 2002.
11. *Facilitation of Keloid healing with CM101/GBS toxin*. C.G. Hellerqvist, B.D. Wamil, M. Neeman and R. Abramovitch, U.S. 6,569,838 - May 27, 2003.
12. *Facilitation of Wound Healing with CM101/GBS Toxin*. C.G. Hellerqvist, B.D. Wamil, M. Neeman and R. Abramovitch, U.S. 6,670,337 – December 30, 2003.
13. *GBS Toxin Receptor.(HP59 peptide sequences)* C.G. Hellerqvist and Changlin Fu. U.S. 6,803,448 – October 12, 2004
14. *GBS Toxin Receptor. (HP59 as a drug and antibody target)* C.G. Hellerqvist and Changlin Fu. U.S. 2005-0002931-A1 January 6, 2005

Pending Patents:

1. *GBS Toxin Receptor Protein and DNA Sequences*. C.G. Hellerqvist and C. Fu. U.S. Patent Application Serial No. 60/093,843. Total of 12 anticipated patents.

2. *Methods for Preventing or Attenuating Pathoangiogenic Conditions*. C.G. Hellerqvist. U.S. C0779-2062.

Book Chapters:

1. Studies on Some Salmonella Lipopolysaccharides. Akademisk avhandling. Stockholm University. C.G. Hellerqvist (1971).
2. Cell Adhesion. C.G. Hellerqvist, W.L. Rottman, B.T. Walter and S. Roseman. Los Alamos Symposium, "Mammalian Cells Probes and Problems," C.R. Richmond, D.F. Peterson, P.R. Mulancy and E.C. Anderson, Editors. ERDA Symp. Series, (1975) Springfield, Va., National Technical Information Service.
3. A Collagenous Component of the Microexudate Carpet Secreted by Attaching Human Fibroblasts. C.E. Schwartz, C.G. Hellerqvist and L.W. Cunningham, Ann. N.Y. Acad. Sci. 312, 450 (1978).
4. Biosynthetic Matrices from Cells in Culture. C.G. Hellerqvist. Methods in Enzymology. L.W. Cunningham, Ed. 82, 530 (1982).
5. Lung Injury by Streptococcal Toxins. H.W. Sundell, W. Fish, K. Sandberg, K.E. Edberg, R.S. Pappas and C.G. Hellerqvist. Vanderbilt University Press (1989).

Honors:

- | | |
|------|--|
| 1968 | Nils Lofgrens Award for Excellence in Biomedical Research |
| 1969 | Nils Lofgrens Award for Excellence in Biomedical Research |
| 1970 | Nils Lofgrens Award for Excellence in Biomedical Research |
| 1971 | Sigrid Arhenius Award for the Highest Rated Thesis Defended at the Faculty of Science at Stockholm University |
| 1971 | Titular Docent of Honor, Stockholm University |
| 1972 | Special Fellow of the Jane Coffin Childs Memorial Foundation for Medical Research |
| 1979 | CITATION CLASSIC. Carl G. Hellerqvist. In Agriculture, Biology and Environmental Sciences <u>10</u> #51 for "Structural Studies on the O-Specific Side-Chains of the Cell-Wall Lipopolysaccharide from <i>Salmonella typhimurium</i> 395 MS. C.G. Hellerqvist, B. Lindberg, S. Swensson, T. Holme and A.A. Lindberg. Carbohydr. Res. 8:43 (1968). |
| 1982 | FASEB Travel Award to Australia |
| 1992 | CITATION CLASSIC. Björndal, H., Hellerqvist, C. G., Lindberg, B., and Svensson, S. In Physical, Chemical, and Earth Science <u>6</u> #4 for "Methylation |

- 2004 Analysis of Polysaccharides. H. Bjorndal, C.G. Hellerqvist, B. Lindberg and S. Swensson. *Angew. Chemie* 82:643 (1970).
 Invited as one of 100 International Investigators to the International Campaign for Cures for spinal cord injury Paralysis (ICCP) Clinical Trials Workshop.

Memberships:

The Society for Neuroscience
 American Association for Cancer Research
 American Society of Clinical Oncology
 Wound Healing Society
 Drug Information Association
 Society for Glycobiology (formerly Society for Complex Carbohydrates International Society, 700 members - Elected Secretary 1987-93)

Meetings:

Organized the 21st Annual Meeting of the Society for Complex Carbohydrates; 36 lecturers, 8 sessions, 280 registered participants, Nashville, Tennessee, November 11 - 14, 1992.
 Co-Organizer of the Annual Meeting of the Society for Glycobiology, South Bend, Indiana, November 1993.
 Co-Organizer of the XIII International Symposia on Glycoconjugates, Seattle, Washington, August 20 - 26, 1995.

Reviewer for:

NIH, Special Study Session on Angiogenesis.
 NSF
 Journal of Biological Chemistry
 Carbohydrate Research
 In Vitro
 Analytical Biochemistry
 Biochemistry
 Oncology Research
 Journal of the National Cancer Institute

Invited Lectures and Chaired Sessions:

- July 19, 2004 VICC Host Tumor Interaction Seminar. “ HP59 the target protein for CM101 in pathoangiogenesis and diagnostics. Is there a basis for the concept pathoangiogenesis?”
- April 2002 Shenzhen Medical School, China. Medicine Grand Rounds
 “Pathoangiogenesis – A Key to Treatment of Cancer, Wounds, Trauma, and

	Inflammatory Diseases. Potentials for CM101 and its Target Protein HP59"
December 2001	Shanghai Institute for Pharmaceutical Industry, China. "Therapeutic Potentials for CM101 in Cancer and inflammatory diseases".
June 2001	Angiogenesis: Basic Science and Clinical Development, Crete, Greece
January 2001	Vanderbilt University, Nashville, Tennessee Grand Rounds in Medicine:
December 2000	University of Texas Medical Branch, NIEHS Center, Galveston, Texas: "CM101 and its receptor HP59 in pathoangiogenic disease processes"
November 2000	University of Louisiana, Baton Rouge: "CM101 and HP59: Potential Clinical Applications"
August 2000	International Carbohydrate Symposia, Hamburg, Germany: "Studies on CM101 and its target receptor HP59 in pathoangiogenic dependent disease processes"
April 2000	ACS Lecture, Middle Tennessee State University, Murfreesboro, Tennessee
November 1999	Karolinska Institute, Stockholm, Sweden: "Anti-Pathoangiogenics: Drugs for the Future"
November 1999	Angiogenesis Conference (International Business Communications): "CM101: An Anti-Pathoangiogenic Agent and its Receptor CM201 - Areas of Application"
October 1999	Society for Neuroscience 29 th Annual Meeting: "Recovery of Neurologic Function with CM101 Treatment after Surgical Removal of Gliosis in Chronic Spinal Cord Injury"
October 1999	Angiogenesis '99, London, England: "CM101: An Anti-Pathoangiogenic Agent and its Receptor CM101 - Areas of Applications"
August 1999	Glyco XV: "CM101-Mediated Recovery of Walking Ability in Adult Mice Paralyzed by Spinal Cord Injury"
July 1999	NATO/ASI - Angiogenesis: From the Molecular to Integrative Pharmacology, Crete, Greece: "CM101: An Anti-Pathoangiogenic Polysaccharide - Harnessing a Powerful Array of Biological Effects"
May 1999	Karolinska Institute, Stockholm, Sweden: "Recovery of Neurologic Function with CM101 Treatment after Surgical Removal of Gliosis in Chronic Spinal Cord Injury"
May 1999	Paris / Milan / Berlin Lectures to Pharmaceutical companies

- March 1999 Angiogenesis - Novel Therapeutic Development, Boston, Massachusetts: "CM101: An Anti-Pathoangiogenic Agent and its Receptor CM201 - Areas of Application"
- November 1998 1st International Conference on Biological Therapy and Modern Cancer Therapy, Guangzhou and Hong Kong, China: "CM101: An Anti-Pathoangiogenic Polysaccharide Reduces Immunoprivilege of Tumors"
- November 1998 Glycocompounds 98, Vancouver, British Columbia: "CM101: An Anti-Pathoangiogenic Polysaccharide - Harnessing a Powerful Array of Biological Effects"
- October 1998 Impact of Biotechnology on Prediction, Prevention and Treatment, Nice, France: "CM101: An Anti-Pathoangiogenic Polysaccharide Reduces Immunoprivilege of Tumors"
- September 1998 Acute Neuronal Injury: New Therapeutic Opportunities, Las Vegas, Nevada
- August 1998 19th International Carbohydrate Symposium, San Diego, California: "CM101: An Anti-Pathoangiogenic Polysaccharide -Harnessing a Powerful Array of Biological Effects"
- June 1998 10th NCI-EORTC Symposium on New Drugs in Cancer Therapy, Amsterdam, The Netherlands: "An Anti-Pathoangiogenic Polysaccharide Induces Apoptosis in Adenocarcinoma Metastasis"
- May 1998 International Glyco-BioTechnology Symposium, Braunschweig, Germany: "CM101: An Anti-Pathoangiogenic Polysaccharide - Harnessing a Powerful Array of Biological Effects"
- April 1998 IBC's 4th Annual Conference on Angiogenesis, Boston, Massachusetts: "CM101 - An Anti-Pathoangiogenic Agent: Clinical and Preclinical Experiences"
- March 1998 Keystone Symposia on Molecular Biology of the Cardiovascular System, Steamboat Springs, Colorado: "Clinical and Pre-Clinical Studies on CM101, an Anti-Pathoangiogenic Agent"
- October 1997 CHI - Angiogenesis Antagonists: Current Clinical Trials, Drug Development, and Regulatory Issues, Hamilton, Bermuda
- July 1997 Mount Sinai Grand Rounds, New York, New York: "CM101: The Evolution of an Anti-Pathoangiogenic Agent from a Neonatal Pathogen"
- June 1997 NATO-Advanced Study Institute on Angiogenesis: Models, Modulators and

Clinical Applications, Kos, Greece: "Clinical Development and Mode of Action of CM101 as an Anti-Tumor Agent Targeting the Neovasculature"

- April 1997 ACS Symposium on Carbohydrate-Based Anti-Inflammatory Chemotherapy, San Francisco, California: "Clinical and Preclinical Evidence for a Mechanism of Action of CM101 - An Anti-Tumor Agent Targeting Pathogenic Neovasculature"
- February 1997 IBC Third Annual Conference on Angiogenesis, Boston, MA: "Evolution of an Anti-Neovascularization Agent from a Neonatal Pathogen"
- February 1997 AACR Meeting on Cell Signaling and Cancer Treatment, Telfs-Buchen, Austria: "Clinical and Preclinical Evidence for a Mechanism of Action of CM101 - An Anti-Tumor Agent Targeting Pathologic Neovasculature"
- October 1996 Third International Symposium on Impact of Cancer Biotechnology, Nice, France: "CM101 - AntiTumor Activity and Mechanism of Action as an Anti-Neovascularization Agent"
- October 1996 Third International Symposium on Impact of Cancer Biotechnology, Nice, France (*Chairman, Session on "Angiogenesis"*)
- August 1996 Sixth World Congress for Microcirculation, Munich, Germany: "Evolution of an Anti-Neovascularization Agent from a Neonatal Pathogen"
- April 1996 Third Annual Angiogenesis Antagonists (CHI), Boston, MA (*Chairman, Session on "Clinical Trial Updates"*)
- April 1996 Third Annual Angiogenesis Antagonists (CHI), Boston, MA: "CM101: Clinical Evidence for Mechanism of Action as an Anti-Neovascularization Agent"
- February 1996 Weizmann Institute of Science, Rehovot, Israel: "Molecular Pathophysiology and Clinical Development of CM101-GBS Toxin: an Anti-Neovascularization Agent in Anti-Cancer Treatment"
- February 1996 Hadassah Medical Organization, Jerusalem, Israel: "Evolution of an Anti-Neovascularization Agent from a Neonatal Pathogen"
- February 1996 Tel Aviv University, Tel Aviv, Israel: "Preclinical and Clinical Evidence for a Mechanism of Action of CM101 - An Anti-Tumor Agent Targeting Pathologic Neovasculature"
- February 1996 Gordon Conference on Drug Carriers in Medicine and Biology, Ventura, Californi
- October 1995 Karolinska Institute, Center for Microbiology and Tumor Biology, Stockholm, Sweden: "Molecular Pathophysiology and Clinical Development of CM101-

GBS Toxin: An Anti-Neovascularization Agent in Anti-Cancer Treatment"

- October 1995 University of Upsala, Upsala, Sweden: "Molecular Pathophysiology and Clinical Development of CM101-GBS Toxin: An Anti-Neovascularization Agent in Anti-Cancer Treatment"
- October 1995 University of Gothenburg, Gothenburg, Sweden: "Molecular Pathophysiology and Clinical Development of CM101-GBS Toxin: An Anti-Neovascularization Agent in Anti-Cancer Treatment"
- October 1995 University of Stockholm, Dept. of Organic Chemistry, Lund, Sweden: "Molecular Pathophysiology and Clinical Development of CM101-GBS Toxin: An Anti-Neovascularization Agent in Anti-Cancer Treatment"
- October 1995 Lund University, Dept. of Medical Microbiology, Lund, Sweden: "Molecular Pathophysiology and Clinical Development of CM101-GBS Toxin: An Anti-Neovascularization Agent in Anti-Cancer Treatment"
- September 1995 The Vanderbilt Cancer Center, Nashville, Tennessee: "Evolution of an Antitumor Agent from a Neonatal Pathogen"
- August 1995 Gordon Conference on Angiogenesis and Microcirculation, Newport, Rhode Island: "Evolution of an Anti-Neovascularization Agent from a Neonatal Pathogen"
- August 1995 XIII International Symposia on Glycoconjugates, Seattle, Washington (*Chairman, Session on "Role of Glycoconjugates in Bacterial and Viral Infections"*)
- August 1995 XIII International Symposia on Glycoconjugates, Seattle, Washington; "The Evolution of an Anti-Tumor Agent from a Neonatal Pathogen"
- August 1995 XIII International Symposia on Glycoconjugates, Seattle, Washington (*Chairman, Plenary Lecture on Microbial Adhesion*)
- July 1995 7th European Workshop Conference on Bacterial Protein Toxins, Hindsgal, Middelfart, Denmark: "The Evolution of an Anti-Neovascularization Agent from a Neonatal Pathogen"
- July 1995 19th International Congress of Chemotherapy, Montreal, Quebec, Canada: "Systemic Cytokine Levels in Cancer Patients Receiving the Anti-Neovascularization Drug CM101"
- June 1995 3rd NATO Advanced Study Institute on Angiogenesis, Porto Carras, Greece:

"CM101: Pre-clinical and Clinical Evidence for Targeting Pathologic Neovasculature in Tumors"

- June 1995 3rd NATO Advanced Study Institute on Angiogenesis, Porto Carras, Greece
(*Chairman, Session on "Inhibitors of Angiogenesis"*)
- May 1995 Glycoday III, Annapolis, Maryland
- May 1995 Advances in Glycotechnology, San Diego, CA: "Carbohydrates in the Clinic"
- April 1995 New Cancer Strategies: Angiogenesis Antagonists, Washington, DC
(*Chairman, Session on "Clinical Results"*)
- April 1995 New Cancer Strategies: Angiogenesis Antagonists, Washington, DC:
"CM101: Evidence for Targeting Tumor Neovascularization"
- March 1995 National Institutes of Health - Angiogenesis Group, Washington, DC
- February 1995 Harvard Medical School, Boston, Massachusetts: "The Evolution of an Anti-
Neovascularization Agent from a Neonatal Pathogen"
- February 1995 Harvard Medical School, Oncologic Nuclear Medicine, Joint Program in
Nuclear Medicine Conference, Boston, Massachusetts: "The Evolution of an
Anti-Tumor Agent from a Neonatal Pathogen"
- 1994 Cancer Clinical Trials: New Challenges in Cancer Research, Philadelphia,
Pennsylvania: "CM101 (GBS Toxin): Clinical Evidence for a Tumor-
Targeted Induction of Inflammation"
- 1994 Johns Hopkins University, Department of Pharmacology and Molecular
Sciences: "Evolution of an Anti-Tumor Agent from a Neonatal Pathogen"
- 1994 Johns Hopkins School of Medicine: "Clinical Evaluation of a Bacterial
Polysaccharide as an Anti-Tumor Agent"
- 1994 Society for Leukocyte Biology, Tucson, Arizona: "Preliminary Results of a
Phase I Trial of CM101 in Cancer Patients"
- 1994 9th Mediterranean Congress of Chemotherapy, Milan, Italy; "CM101 (GBS
Toxin): Preclinical and Clinical Evidence for a Tumor-Targeted Induction of
Inflammation"
- 1994 Glycoday II, Annapolis, Maryland: "Glycobiology Cures Cancer"
- 1994 The Second Annual Conference on Glycotechnology, San Diego, California:
"Developments in Clinical and Basic Science of CM101"

- 1993 Complex Carbohydrates in Biology and Medicine, Frisco, Colorado: "Evolution of an Anti-Tumor Agent from a Neonatal Pathogen"
- 1994 Glycotechnology -- Development and Commercialization of Carbohydrate-Based Therapeutics, International Business Communications, Washington, DC (*Chairman, Session on "Applications - Clinical and Pre-Clinical Results"*)
- 1994 Glycotechnology -- Development and Commercialization of Carbohydrate-Based Therapeutics, International Business Communications, Washington, DC: "Evolution of an Anti-Tumor Agent from a Neonatal Pathogen"
- 1993 22nd Annual Meeting of the Society for Complex Carbohydrates, San Juan, Puerto Rico: "Evolution of an Anti-Tumor Agent from a Neonatal Pathogen"
- 1993 22nd Annual Meeting of the Society for Complex Carbohydrates, San Juan, Puerto Rico (*Chairman, Special Session*)
- 1993 New Cancer Strategies: Angiogenesis & Angiogenesis Antagonists, Cambridge Healthtech Institute: "GBS Toxin: From Neonatal Pathogen to Anti-Tumor Agent" (*Chairman*)
- 1993 Institut für Organische Chemie und Biochemie, Universität, Bonn, Bonn, Germany: "Evolution of an Anti-Tumor Agent from a Neonatal Pathogen"
- 1993 Glaxo Research Institute, Research Triangle Park, North Carolina: "GBS Toxin, A Novel Anti-Tumor Agent"
- 1993 International Symposium on Glycoconjugates (Glyco XII), Kraków, Poland: "GBS Toxin: An Inflammatory Agent With Anti-Tumor Activity"
- 1993 NATO/ASI - Angiogenesis: Molecular Biology, Clinical Aspects, Rhodes, Greece: "Anti-Tumor Effects of GBS Toxin are Caused by Induction of a Targeted Inflammatory Reaction"
- 1993 18th International Congress of Chemotherapy, Stockholm, Sweden: "Anti-Tumor Effects of GBS Toxin: Caused by Induction of a Targeted Inflammatory Reaction"
- 1993 Pulmonary Medicine Conference, Vanderbilt University: "GBS Toxin: A Potential Anti-Metastatic Agent"
- 1993 Neonatal-Pulmonary Research Conference, Vanderbilt University: "GBS Toxin: A Potential Anti-Metastatic Agent"
- 1993 Clinical Research Center, Harrow, England: "GBS Toxin: A Potential Anti-Metastatic Agent"

- 1994 Cancer Research Campaign, Gray Laboratory, Northwood, England: "GBS Toxin: A Potential Anti-Metastatic Agent"
- 1993 Zeneca (ICI), Manchester, England: "GBS Toxin: A Potential Anti-Metastatic Agent"
- 1993 Georgetown University, Department of Cell Biology, Washington, DC: "GBS Toxin: A Potential Anti-Metastatic Agent"
- 1993 22nd Annual Keystone Symposium, Silverthorne, Colorado: "Anti-Tumor Effects of GBS Toxin are Caused by Induction of a Targeted Inflammatory Reaction"
- 1992 Grand Rounds, Department of Pathology, Vanderbilt University: "GBS Toxin: A Potential Anti-Metastatic Agent"
- 1992 21st Annual Meeting of the Society for Complex Carbohydrates, Nashville, Tennessee, U.S.A.: "Anti-Tumor Effects of GBS Toxin are Caused by Induction of a Targeted Inflammatory Reaction"
- 1992 XVIth International Carbohydrate Symposium on Carbohydrate Chemistry, Paris, France: "A Micro Analytical Method for Quantitative and Qualitative Carbohydrate Structural Analysis"
- 1991 XVIth International Symposium on Glycoconjugates, Toronto, Canada: "GBS Toxin; From Neonatal Pathogen to Anti-Tumor Agent" 1991 University of Illinois at Chicago: "GBS Toxin; From Neonatal Pathogen to Anti-Tumor Agent"
- 1991 Gordon Research Conference on Molecular Mechanism on Microbial Adhesion: "Mechanism Induction of GBS Induced Inflammatory Response"
- 1989 XV International Symposium on Glycoconjugates, Jerusalem, Israel (*Chairman, Section on "Analytical Techniques"*)
- 1989 Biomembrane Institute, Washington State University, Seattle, WA: "GBS Toxin as a Biological Response Modifier in Cancer Therapy"
- 1989 Milligene Corporation, Bedford, MA: "Sequence Analysis of Carbohydrates"
- 1989 Waters, Millford MA: "Methods in Analytical Carbohydrate Chemistry"

- 1988 University of Michigan, Ann Arbor, MI: "Molecular Basis for Group B Streptococcal Disease"
- 1988 University of Gothenburg, Gothenburg, Sweden: "Group B Streptococcus"
- 1988 International Conference on Carbohydrate Chemistry, Stockholm, Sweden: "Sequence Analysis of Polysaccharides"
- 1988 NIH Division of Carbohydrate Chemistry: "GBS Toxin"
- 1980-87 Invited lectures at Stockholm University, Uppsala University, Ohio State University, University of Miami, and Johns Hopkins University
- 1970-80** Invited lectures at MIT, Berkeley, Stanford, Johns Hopkins, Penn State, Max Plank Freiburg, Pasteur Institute-Paris France, University of Washington, University of Michigan, Michigan State, University of Wisconsin, Mass. General-Harvard, FEBS-Symposium Helsinki Finland, Ohio State, Gordon Conference on Carbohydrates, FASEB Symposium on Cell-Cell Interactions (*Chairman*), and University of Chicago.

Publications:

1. Structural Studies on the O-Specific Side-Chains of the Cell-Wall Lipopolysaccharide from *Salmonella typhimurium* 395 MS. C.G. Hellerqvist, B. Lindberg, S. Svensson, T. Holme and A.A. Lindberg. Carbohyd. Res. 8:43 (1968) (**Citation Classic in 1979**).
2. Methylation Analysis of Polysaccharides. H. Bjorndal, C.G. Hellerqvist, B. Lindberg and S. Svensson. Angew. Chemie 82:643 (1970) (**Citation Classic in 1992**).
3. Structural Studies on the O-Specific Side-Chains of the Cell-Wall Lipopolysaccharide from *Salmonella typhimurium* LT2. C.G. Hellerqvist, B. Lindberg, S. Svensson, T. Holme and A.A. Lindberg. Carbohyd. Res. 9:237 (1969).
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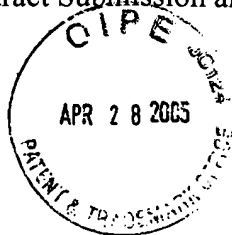
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 86. Expressional Cloning of CM101 Receptor Gene from Mammalian Cells. C. Fu, S. Bardhan, N.D. Cetateanu, E. Shi, H.-P. Yan, C.E. Carter, R.S. Lloyd, C. Venkov, F.M. Yakes, D.L. Page, and C.G. Hellerqvist. American Association for Cancer Research Annual Meeting (1999).
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88. Cytokine-Driven Inflammatory Response to CM101 in Tumor Neovasculature. Carl Hellerqvist, He-Ping Yan, Clint Carter, David Page, Barbara Wamil, F. Michael Yakes, and Gary Thurman. Keystone Symposium - Inflammatory Paradigms and the Vasculature (C4) (1999).
 89. Effects of Estrogen on the Developing Vasculature. C. Venkov, N. Vorobieff, H.-P. Yan, B. Wamil, D. Page, and C. Hellerqvist. Keystone Symposium - Inflammatory Paradigms and the Vasculature (C4) (1999).
 90. Recovery of Neurologic Function with CM101 Treatment after Surgical Removal of Gliosis in Chronic Spinal Cord Injury. C.G.Hellerqvist, A.W. Wamil, B.D. Wamil, F. Sun, and P. Chi. 29th Annual Meeting of the Society for Neuroscience (1999).
 91. Recovery of Neurologic Function with CM101 Treatment after Surgical Removal of Gliosis in Chronic Spinal Cord Injury. C.G.Hellerqvist, A.W. Wamil, B.D. Wamil, F. Sun, and P. Chi. 17th Annual National Neurotrauma Society Meeting (1999).
 92. Identification and Characterization of HP59: A Unique Pathoangiogenic Marker Targeted by CM101. C. Fu, N.D. Cetateanu, S. Bardhan, H.-P. Yan, C.E. Carter, R.S. Lloyd, F.M. Yakes, B.D. Wamil, D.L. Page, and C.G. Hellerqvist. American Association for Cancer Research Annual Meeting (2000).
 93. CM101 Treatment Overrides Tumor-Induced Immunoprivilege Leading to Apoptosis. B.D. Wamil, F.M. Yakes, F. Sun, H.-P. Yan, C.E. Carter, and C.G. Hellerqvist. American Association for Cancer Research Annual Meeting (2000).
 94. CM101 Accelerates Resurfacing by Decreasing Formation of Pathogenic Capillaries and Blood Flow During Cutaneous Wound Repair. L.B. Nanney, B.D. Wamil, J. Whitsitt, N.L. Cardwell, J.M. Davidson, and C.G. Hellerqvist. Wound Healing Society Educational Symposium (2000).
 95. Effects of the Anti-Angiogenic Agent CM101 Following Optic Nerve Crush in the Adult Rat. M. Ohlsson, P. Mattsson, B.D. Wamil, C.G. Hellerqvist, and M. Svensson. Society for Neuroscience Annual Meeting (2000).
 96. Effect of CM101 Plus Methylprednisolone on the Recovery from Paralysis. B.D. Wamil, A.W. Wamil, and C.G. Hellerqvist. Society for Neuroscience Annual Meeting (2000).
 97. CM101 Treatment Promotes GAP-43 Positive Axonal Regrowth Following Chronic Spinal Cord Injury. C.G. Hellerqvist, H.-P. Yan, P. Chi, F. Sun, A.W. Wamil, and B.D. Wamil. Society for Neuroscience Annual Meeting (2000).
 98. The CM101 Target Protein HP59 is a Pathoangiogenic Marker with Potential as a Vaccine and Drug Target. Barbara D. Wamil, Yufen Wang, Fenglei Sun, He-Ping Yan, and Carl G.

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100. Effects of the Anti-Angiogenic Agent CM101 Following Complete Spinal Cord Injury in the Adult Rat. M. Ohlsson, P. Mattsson, C.G. Hellerqvist, I.A. Langmoen, B. Meijer, M. Svensson. Society for Neuroscience Meeting (2001).
101. Vaccines based on the CM101 target protein HP59 protects against pathoangiogenesis and tumor growth with no effect on reproduction. B.D. Wamil, Y. Wang, C. Fu, H. Yan, C.G. Hellerqvist, AACR_NCI_EORTC International Conference on Molecular Targets and Cancer Therapeutics (2001)
102. A Cancer Vaccine Based on the Pathoangiogenic Marker HP59 Induces a Cellular Immune Response Protecting Against Metastases Following I.V. Melanoma Infusions in Mouse Models. B.D. Wamil, Y. Wang, L. Geng, D. Hallahan, and C.G. Hellerqvist. AACR Conference on Frontiers in Cancer Prevention Research.(2002) Poster Discussion Session.
103. CM101 treatment in Acute, and coupled with Stem cells in Chronic Paralysis, C. G. Hellerqvist, B.D. Wamil and A.W. Wamil. ICCP Clinical Trials Workshop on Spinal Cord Injury, (2004) Workshop presentation.



96th Annual Meeting
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Session ID: Immunology 6
Session Title: Tumor Vaccines 1
Session Type: Poster Session
Sponsored by:
Session Start: 4/18/2005 1:00:00 PM
Session End: 4/18/2005 5:00:00 PM
Location: Exhibit Hall B-D, Anaheim Convention Center
Section Number: 30

Presentations:

3440--Monday, 1:00 p.m. - 5:00 p.m.--Preliminary hyperexpansion of mouse CD34^{pos} stem cells provides multipotent dendritic cell (DC) precursors for tumor-DC hybridization and active immunization

3441--Monday, 1:00 p.m. - 5:00 p.m.--Manufacturing process of a dendritic cell vaccine for colorectal cancer phase I/II trial.

3442--Monday, 1:00 p.m. - 5:00 p.m.--Enhancement of DNA vaccine potency by co-administration of mature dendritic cells pulsed with a Pan-MHC class II peptide

3443--Monday, 1:00 p.m. - 5:00 p.m.--Modulation of tumor-derived exosomes for an efficient cancer vaccine

3444--Monday, 1:00 p.m. - 5:00 p.m.--Fusion process and fusion efficiency is essential to optimal antitumor immunity

3445--Monday, 1:00 p.m. - 5:00 p.m.--Screening of peptides that mimic MUC1 carbohydrate epitope as candidates for cancer vaccine

3446--Monday, 1:00 p.m. - 5:00 p.m.--MUC1-specific immune therapy is successful in rejecting colon cancer tumor cells in a MUC1-tolerant host

3447--Monday, 1:00 p.m. - 5:00 p.m.--Induction of a CD8+ T cell response to HPV16 E2 in HLA-A2 transgenic mice

3448--Monday, 1:00 p.m. - 5:00 p.m.--Antitumor activity human papillomavirus Type 16 E7-specific T cells in patients with virally infected squamous cell carcinoma of the head and neck (SCCHN)

3449--Monday, 1:00 p.m. - 5:00 p.m.--Induction of CD8 T lymphocytes specific for the recognition of a breast cancer-associated polymorphism in the HER2/neu protein in a clinical trial with the HER2 E75-peptide vaccine.

3450--Monday, 1:00 p.m. - 5:00 p.m.--Level of HER-2/neu protein expression in primary breast cancer may impact the development of HER-2/neu-specific endogenous immunity.

3451--Monday, 1:00 p.m. - 5:00 p.m.--Reduction of regulatory T cell levels and enhanced antitumor immune responses in breast cancer patients receiving a HER2 peptide (E75) vaccine.

3452--Monday, 1:00 p.m. - 5:00 p.m.--Serum cytokine levels in breast cancer patients before and after receiving a HER2/neu vaccine assessed using multiplex technology.

3453--Monday, 1:00 p.m. - 5:00 p.m.--Vaccination of rat HER-2/neu transgenic mice, with syngeneic rat HER-

2/neu, but not with xenogenic human ErbB receptors, prevents the development of spontaneous mammary carcinomas.

3454--Monday, 1:00 p.m. - 5:00 p.m.--Genetic immunization against rat HER2/neu in tumor challenge and spontaneous mouse tumor models

3455--Monday, 1:00 p.m. - 5:00 p.m.--Induction of effective and antigen-specific antitumor immunity by novel protein- and peptide-based ErbB2/HER2 vaccines

3456--Monday, 1:00 p.m. - 5:00 p.m.--Melanoma patients treated with an autologous dendritic cell vaccine demonstrate tumor reactive antibodies

3457--Monday, 1:00 p.m. - 5:00 p.m.--CD4⁺ and CD8⁺ T cells responding to dendritic cells transfected with *in vitro* transcribed (IVT)-RNA encoding melanoma antigen Melan-A/MART-1

3458--Monday, 1:00 p.m. - 5:00 p.m.--The clinical implication of expressions of melanoma antigen gene(MAGE) and synovial sarcoma on Xchromosome (SSX) genes in ovarian malignancies

3459--Monday, 1:00 p.m. - 5:00 p.m.--Use of ultraviolet-irradiated multiple myeloma cells as immunogens to generate tumor-specific cytolytic T lymphocytes

3460--Monday, 1:00 p.m. - 5:00 p.m.--Phase I clinical trial of VACCIMEL plus GM-CSF in melanoma patients stages IIB, III and IV.

3461--Monday, 1:00 p.m. - 5:00 p.m.--Generating human immune responses in humanized SCID/bg mice with U251MG glioma cells expressing the membrane form of macrophage colony stimulating factor (mM-CSF)

3462--Monday, 1:00 p.m. - 5:00 p.m.--Whole-cell lung cancer vaccine: Clinical experience with 27 patients

3463--Monday, 1:00 p.m. - 5:00 p.m.--Novel vaccine immunotherapy for B-cell malignancies using adenoviral delivery of α Galactosyltransferase gene

3464--Monday, 1:00 p.m. - 5:00 p.m.--Induction of specific antitumoral immunity in cancer patients with a dendritic cell (DC)- based protocol. A feasibility study

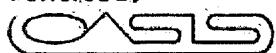
3465--Monday, 1:00 p.m. - 5:00 p.m.--A pilot study of dendritoma vaccine for stage IV renal cell carcinoma

3466--Monday, 1:00 p.m. - 5:00 p.m.--A pilot study of peripheral blood dendritic cells (PBDC) pulsed with NY-ESO-1 ISCOMATRIX® vaccine (ESO/IMX) in patients with treated cancer and minimal residual disease at high risk of relapse

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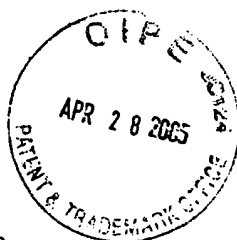
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Session ID: Immunology 10
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Session Type: Poster Session
Sponsored by:
Session Start: 4/19/2005 1:00:00 PM
Session End: 4/19/2005 5:00:00 PM
Location: Exhibit Hall B-D, Anaheim Convention Center
Section Number: 31

Presentations:

5147--Tuesday, 1:00 p.m. - 5:00 p.m.--A comparative analysis of tumor immunity induced by peptide or cell-based vaccination.

5148--Tuesday, 1:00 p.m. - 5:00 p.m.--Induction of an antigen cascade by diversified subcutaneous/intratumoral vaccination is associated with antitumor responses

5149--Tuesday, 1:00 p.m. - 5:00 p.m.--Antigen specific T-cell responses following whole tumor cell vaccination

5150--Tuesday, 1:00 p.m. - 5:00 p.m.--Preclinical evaluation of fully synthetic unimolecular penta-antigenic carbohydrate antigen as a cancer vaccine

5151--Tuesday, 1:00 p.m. - 5:00 p.m.--Ganglioside GD1a, present in Ovarian Cancer cells, Ascites and Sera of patients elicits endogenous IgM response.

5152--Tuesday, 1:00 p.m. - 5:00 p.m.--A DNA-based cancer vaccine activates both innate and adaptive immunity by engaging the NKG2D receptor

5153--Tuesday, 1:00 p.m. - 5:00 p.m.--A novel stress protein, legumain, is a target for a genetic vaccine against breast cancer

5154--Tuesday, 1:00 p.m. - 5:00 p.m.--Recombinant *Listeria* induce and boost antigen-specific immune responses in the presence of *Listeria*-specific cellular and humoral immunity

5155--Tuesday, 1:00 p.m. - 5:00 p.m.--Immunization with genetic vectors expressing rhesus CEA efficiently breaks immune tolerance in mice and rhesus monkeys.

5156--Tuesday, 1:00 p.m. - 5:00 p.m.--Does adenoviral vector replicative capacity influence the efficiency of antigen-specific immune response induction by Ad-transduced dendritic cells?

5157--Tuesday, 1:00 p.m. - 5:00 p.m.--Development of a whole cell vaccine for acute myeloid leukaemia: a comparison of B7-1, B7-2 and 4-1BBL

5158--Tuesday, 1:00 p.m. - 5:00 p.m.--Evaluation of a poxvirus vaccine target human p53 in a novel murine model

5159--Tuesday, 1:00 p.m. - 5:00 p.m.--Immunogenic and antitumor efficiency of plasmid DNA and Adenovirus vectors encoding CEA fusion proteins.

5161--Tuesday, 1:00 p.m. - 5:00 p.m.--Vaccination with sulfhydryl-based idiotypic-carrier protein conjugates elicits

therapeutic anti-tumor immunity superior to glutaraldehyde conjugates in the A20 murine lymphoma model.

5162--Tuesday, 1:00 p.m. - 5:00 p.m.--Immunization of Rhesus monkeys with a conjugate vaccine IGN402 induces immune responses against carbohydrate and protein antigens, and cancer cells: correlation with cytokine release

5163--Tuesday, 1:00 p.m. - 5:00 p.m.--Preclinical evaluation of an hGM-CSF DNA-cationic lipid complexed autologous tumor cell vaccine using dogs with spontaneously arising non-Hodgkin's lymphoma as a model

5164--Tuesday, 1:00 p.m. - 5:00 p.m.--Temporal induction of a beneficial inflammatory cytokine milieu relative to peptide vaccination is crucial for the optimal adjuvanticity of the TLR3 agonist polyinosinic-polycytidylic acid (Poly I:C)

5165--Tuesday, 1:00 p.m. - 5:00 p.m.--High affinity MHC class II epitopes can be accurately predicted with publicly available algorithms

5166--Tuesday, 1:00 p.m. - 5:00 p.m.--Potent tumor-specific immunity induced by an *in vivo* heat shock protein-suicide gene based tumor vaccine

5167--Tuesday, 1:00 p.m. - 5:00 p.m.--The endogenous danger signaling molecule, uric acid, converts immunity from non-protective to protective when used as a vaccine adjuvant.

5168--Tuesday, 1:00 p.m. - 5:00 p.m.--Mechanism of antitumor immunity induced by an anti-idiotypic antibody pulsed dendritic cells vaccine in a murine model transgenic for human carcinoembryonic antigen (CEA)

5169--Tuesday, 1:00 p.m. - 5:00 p.m.--Chaperone-rich cell lysate (CRCL) possesses a high carrying capacity for antigenic peptides leading to enhanced CTL activation

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A cancer vaccine based on the pathoangiogenic marker HP59 gives a cellular immune response protecting against repeated i.v. melanoma infusions in mouse models.

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We recently reported the expression cloning of HP59, (Gen Bank AF 244 577) the human target protein for CM101/GBS toxin (1), a bacterial toxin derived from culture media of Group B Streptococcus. CM101/GBS toxin, able to induce respiratory distress in an animal model, has been isolated and identified from body fluids of newborn babies suffering from respiratory distress (2). CM101 in the clinic induced an inflammatory response targeting only tumor vasculature (3,4) and induced an inflammatory reaction which, effectively broke down the tumor immuno privilege (5). The HP59 protein was shown by immunohistochemistry (IHC) to be present in neonatal lung endothelium for less than 8 days after birth consistent with the pathophysiology of GBS infections in the newborn baby (2). HP59 was shown by IHC to be present also in pathologic human tumor vasculature but not in the normal vasculature suggesting that the protein may be critical to embryogenic and pathologic angiogenesis (1). Mice and humans share the age dependent susceptibility to GBS infections and the monoclonal antibodies (mAb) generated to HP59 or the sheep homologue SP55 (87%) (AF 244578) derived peptides stained pathologic vasculature also in mice. HP59 has a unique 41 amino acid (aa) sequence at the N-terminal with no homology to any human protein and the peptide H3 used below as a single immunogen is composed of aa 8-28. The uniqueness of HP59 to pathologic vasculature led us to test KLH conjugated synthetic peptides based on the HP59 and SP55 sequences as a vaccine against cancer. C57 mice were immunized with a mixture of three HP59 (H1 aa 50-63, H2 aa 112-125 and H3 aa 8-28) and two SP55 (P56 aa 9-35, P57 aa 71-84) derived peptides (100µg each) in Complete Freud's Adjuvant (CFA) twice over two weeks followed by immunizations with peptides alone in Incomplete CFA (ICFA). Seven male and five female mice were inoculated s.c. with Lewis Lung tumor cells. Five each of control mice were immunized with CFA and ICFA alone. Immunization resulted in a 62% attenuation of tumor growth ($p=0.025$) in the immunized mice (1). IHC analysis of tumor tissues demonstrated that the inhibition of tumor growth was due to inhibition of both the pathoangiogenesis and the

vasculogenesis processes in the tumor, evidenced by lack of both HP59 and CD34 positive vessels. In this study we show that female mice immunized with the same mixture of HP59 and SP55 peptides became resistant to i.v. infusions of melanoma cell suspensions (1,000 cells in 100µl PBS) repeated on days 1, 140 and 290. The control immunized mice died between days 45 and 101. One immunized mouse died on day 41 with no signs of cancer. The remaining 4 lived until sacrificed after >700 days. These female tumor resistant mice gave birth to normal size litter up to three times, demonstrating the specificity of HP59 to pathologic but not physiologic angiogenesis and vasculogenesis. The immunized mice outlived the mock-immunized mice by >600 days and none had tumor metastases develop in the lungs, which was common to all mock-immunized mice. All mice immunized with the mixture of five peptides P56, P57, H1, H2 and H3 showed a high antibody titer only to P56 (the sheep homologue), which was passed to the off-spring. If antibodies to P56 were inhibitory to tumor angiogenesis then the antibody should be lethal to the offspring by reacting with the lung vasculature in the newborn mice. This was not the case. To confirm that the humoral response was of little consequence groups of 12 C57 mice were immunized with P56 or with adjuvant alone according the protocol used with the mixed peptides. As previously, P56 gave an antibody titer by the sixth week at which time the mice were challenged with s.c. injections with 50,000 Lewis Lung tumors. The excellent immunogen P56 conjugated to KLH gave no attenuation of tumor growth compared to control in the s.c. Lewis Lung model (Data not shown). Likewise in the same model immunization with the human homologue H4 (human equivalent of P56) gave no attenuation of s.c. Lewis Lung tumor growth and vascularization (Data not shown). The mice immunized with the human peptides H2 and H3 and the KLH controls were challenged i.v. with 1,000 melanoma cells in 100µl PBS one week after the last immunization at which time the serum showed no titer for the antibodies. Immunization with individual peptides showed that H3, a unique 21 aa sequence at the N-terminal of HP59 (aa 8-28,) gave immunoprotection, evidenced by significant life extensions ($P < 0.001$) in female and male C57 mice challenged with i.v. infusions of 1,000 melanoma cells on day 1 and 5,000 on day 60. To demonstrate a cellular immunity naive C57 mice, with subcutaneous windows containing readily observable B16 melanoma tumors, were transfused with white cells, which were isolated from the tumor resistant female mice, from the multiple antigen group, after the mice had been injected with a saturated solution of Rhodamine G6. The fluorescent donor T-cells accumulated in the melanoma tumor blood vessels within 15 min, extravasated into the tumor and ablated the tumor vasculature and the tumor, validating that the immune response was cellular. Similarly, T-cells obtained from H3 mice

following tumor challenges ablated the melanoma tumors within 24 hours. T-cells from control mice had no effect. These results suggest a therapeutic potential for the CM101 target protein HP59 both as a drug target and a vaccine against pathoangiogenesis and cancer. Supported by AngioPath Inc (CGH, BDW and YW, in which all have a financial interest) by CA 70937, the Lung SPORE (DH) and the Vanderbilt Ingram Cancer Center Fu et al. Clin. Cancer Res.,7: 4182-4194, (2001), (2) Sundell et al, J Pediatrics 137:338-344 (2000), (3) DeVore et al J. Clin. Can. Res. 3:365-372 (1997), (4) Wamil et al, J. Can. Res. Clin. Oncol. 123(3):173-179 (1997), (5) Yakes et al Cancer Research 60:5740-5746 (2000).